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10/535,442	05/19/2005	Stina Roth	014975-119	8832

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
08/10/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/535,442	ROTH ET AL.	
	Examiner	Art Unit	
	STEVEN C. POHNERT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 19-24* is/are pending in the application.

4a) Of the above claim(s) *6,11,12,15 and 19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,13,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/3/2009 has been entered.

Claim status

This action is in response to papers filed 6/3/2009.

Claims 1-15, 19-24 are pending.

Claims 6, 11-12, 15, 19-22 are withdrawn.

Claims 1-5, 7-10, 13, 23-24 are being examined.

The objection to claim 5 has been withdrawn in view of the amendments.

The 112-2nd paragraph rejection has been withdrawn in view of the amendment of the claims.

Claim Rejections - 35 USC § 103-maintained

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-5, 7-10, 13, 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Haselbeck et al (WO01/70955, published September 27, 2001).

Claim 1 is drawn to,"a DNA primer consisting of the sequence identified with SEQ ID NO: 76 and a DNA primer consisting of the sequence identified with SEQ ID NO: 77." Neither the specification nor the prior art set for a limiting definition of "the sequence identified with." Further the claims recite the indefinite identifier "A" before the recitation of "DNA primers." Thus the broadest reasonable interpretation of, "a DNA primer consisting of the sequence identified" is any sequence that can be identified in the SEQ ID NO.

Claim 5 is drawn to, "combination of oligonucleotide probes comprise the sequence identified with SEQ ID NO 24." Neither the specification nor the prior art set for a limiting definition of "the sequence identified with." Thus the broadest reasonable interpretation of, "combination of oligonucleotide probes comprise the sequence identified with SEQ ID NO 24" is any sequence that can be identified in the SEQ ID NO.

With regards to claim 1, Huang teaches a method of identifying species of bacteria in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer that amplify parE and gyrB (see column 6 lines 28-65). Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related

species (see column 15 lines 27-35). The nested probes are thus the equivalents of the probes claimed. Haung further teaches, “In theory, a single pair of primers, one from each flanking consensus sequence, can be used to amplify the signature sequence. However, a highly preferred embodiment includes a multiplicity of primers having sequences corresponding to potential alternate DNA sequences. As is well-known, the genetic code is degenerate, meaning that an individual amino acid may be coded for by as many as 6 different DNA codons (each codon consisting of three adjacent nucleotides). Thus, even though the amino acid sequence of a region of type II topoisomerase from different organisms may be identical, the DNA in those organisms which codes for the region may differ. The PCR technique requires a good match between the DNA primer sequences especially at the 3' end and the DNA to which it binds (Saiki et al.). Thus, to avoid failing to amplify species having such alternate DNA sequences, the set of primers should include variant primers having at least some of the alternate sequences. Moreover, it is desirable that the amino acids in the consensus sequence be coded for by 3 or fewer different codons, especially in the portion immediately adjacent to the signature segment. Obviously, the presence of one or more amino acids having six possible codons drastically increases the number of possible DNA sequences. By choosing the consensus sequences to have amino acids with at most three possible codons (or in an even more preferred embodiment, two possible codons), the number of different oligonucleotide sequences required in the universal primers is kept manageable” (see column 7, line 60 to column 8, line 9). Huang teaches, “It will be recognized that universal primers such as the compositions

described herein can be constructed for any ubiquitous protein having substantially conserved segments adjacent to variable segments. Depending upon the desired application, gene products other than type II topoisomerase might be preferable. Examples of proteins of potential use according to this invention include RNA polymerase and other DNA binding proteins. Where it is desired only to distinguish among very closely related species, a protein common only to such species may be used" (see column 14, lines 46-50). Huang concludes, "it will be apparent how a specific primer pair for any species can be designed by the methods disclosed herein and using a database" (see column 16, lines 50-55).

With regards to claim 2, Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences due to their sequence similarities (see column 14, lines 16-19). Haung further teaches identification of legionella pneumophila (SEQ ID NO 70), which is a bacteria that infects the respiratory tract.

With regards to claim 3, Huang teaches detection of pseudomonase aeruginosa (see figure 9 a).

With regards to claim 4, Haung et al teaches the use of primers of 15 to 36 nucleotides in length (see column 7, lines 22-25).

With regards to claims 23 and 24 Huang et al teaches primers of 24 bases (see SEQ ID NO 206 and SEQ ID NO 207).

Huang does not teach primers identified with SEQ ID NO 76 and 77.

However, Haselbeck et al teaches SEQ ID NO 9244, which contains nucleotides 82 to 101 that comprise SEQ ID NO 76 of instant claims. Haselbeck further teaches

SEQ ID NO 1844, which contains nucleotides 14 to 33 which comprise SEQ ID NO 77. Haselbeck teaches, "The identified or isolated nucleic acids obtained using the PCR primers may contain part or all of the homologous nucleic acids. Because homologous nucleic acids are related but not identical in 25 sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on sequence regions that are either known to be conserved or suspected to be conserved such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers 30 are at least 10 nucleotides, and preferably at least 20 nucleotides in length. More preferably, the PCR primers are at least 20-30 nucleotides in length. In some embodiments, the PCR primers can be more than 30 nucleotides in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same." (see page 232, lines 23-33). Haselbeck teaches multiple nucleic acid sequences that comprise a multiple nucleotides that are broadly interpreted identified by SEQ ID No 24.

With regards to claims 7-9, Haselbeck teaches, "In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by

researchers to help identify optimal drug targets, profile new compounds, and determine disease pathway" (see page 78, lines 1-5).

With regards to claim 10, Haselbeck teaches use of a single stranded labeled probe (see page 231, lines 5-20).

With regards to claim 10, Haselbeck teaches the use of nucleic acid probes to identify microorganism species from clinical specimens (see page 195, line 20). Haselbeck further teaches, "Single stranded labeled cDNAs are prepared for hybridization to the array" (see page 149, line 17)

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Huang with the nucleic acids taught by Haselbeck which comprise sequences identified by SEQ ID NO 76 and 77. The skilled artisan would be motivated to combine the teachings of Huang and Haselbeck because Huang suggests the use of his method with any protein and any sequence in a database for identification of bacteria. The skilled artisan would also be motivated to combine the teachings of Huang and Haselbeck because Haselbeck suggests the use of his method to identify microorganism species.

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use arrays or microarrays in the combined method of Huang and Haselbeck because Haselbeck teaches it allows the detection of multiple gene expression products and thus markers.

The artisan would have a reasonable expectation of success in combining the teachings of Huang and Haselbeck as both teach methods of identifying microorganism by hybridization using methods and techniques known in the art.

Response to arguments

The response asserts that the prior art of record does not render the instant claims obvious as the claims are drawn to,"a DNA primer consisting of the sequence identified with SEQ ID NO: 76 and a DNA primer consisting of the sequence identified with SEQ ID NO: 77." This argument has been thoroughly reviewed but is not considered persuasive as neither the specification nor the prior art set for a limiting definition of "the sequence identified with." Further the claims recite the indefinite identifier "A" before the recitation of "DNA primers." Thus the broadest reasonable interpretation of, "a DNA primer consisting of the sequence identified" is any sequence that can be identified in the SEQ ID NO. Thus the claims are obvious over the prior art of record. It is noted that if applicant intends for the claims to be drawn to primers consisting of SEQ ID NO 76 and 77, the claims should be amended to recite, "said DNA primers comprise the DNA primer consisting of SEQ ID NO 76 and the DNA primer consisting of SEQ ID NO 77.

The response further asserts that the teachings of Haselback are directed to microarrays for gene expression and thus the diagnostic method of the instant invention is not obvious over the combination of Huang and Haselback. These arguments have been thoroughly reviewed but are not considered persuasive as Huang specifically teaches method of identifying species of bacteria in sample and Horseblock is being

used to demonstrate the oligonucleotide probes were known to be attached to a solid support. Further the gene expression profiling of Horseblock is not excluded by the instant claims as they have comprising language.

3. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Haselbeck et al (WO01/70955, published September 27, 2001) as applied to claims 1-5, 7-10, 13, 23-24 above, and further in view of Hogan et al (US Patent 5541308) and Hopewell et al (Journal of Bacteriology (1990), volume 172, pages 3481-3484).

This rejection is drawn to the interpretation claim 5 requires a probe comprising the entire elected sequence of SEQ ID NO 24 or a sequence that is fully complementary to SEQ ID NO 24.

The teachings of Huang and Haselbeck are set forth in paragraph 4 above.

Haung and Haselbeck do not teach the probe of the comprising all or a portion of SEQ ID NO 24.

However, Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches alignment of these variable regions (see column 6 line 67—column 7, line 8). Hogan further teaches probes should be positioned to minimize stability of probe:nontarget hybrids, by avoiding GC rich regions and areas of frequent mutation (see column 7 lines 10-15). Hogan teaches the use of synthetic oligonucleotide probes of 15-50 base pairs (see column 10, lines 40-45). Hogan further teaches maximizing

stability of probe target hybrid, by avoiding long AT sequences and terminating hybrids with G:C base pairing and the appropriate T_m(see column 7 lines 16-19). Hogan further teaches targeting sequences known to have secondary structure issues and probes that are self-complementary should be avoided (see column 7, lines 20-29).

Hopewell teaches sequence of Staphylococcus aureus gyrB, which comprises SEQ ID NO 24, (see figure 3B). Hopewell teaches that quinolone resistant Staphylococcus aureus are a major medical problem and this resistance is due to mutations in the DNA gyrase enzyme (see page 3481, 1st column, 1st paragraph).

Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific hypervariable regions of bacteria and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the sequences provided by Haselbeck using the method described by Hogan and Huang. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The

claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequence taught by Hopewell and the probe design method of Hogan to make probes to detect bacterial species based on the gyrB. The ordinary artisan would thus design a probe comprising SEQ ID NO 24 or complementary to SEQ ID NO 24. The ordinary artisan would be motivated to use the sequence taught by Hopewell to design probes by Hogan's method of probe design to identify mutations that result in quinolone resistance because Hopewell teaches this is a serious medical problem and proper identification would allow efficient treatment. The artisan would have a reasonable expectation of success as the methods are drawn to well known methods of making and analyzing nucleic acids known in the art.

Response to arguments

The response further traverses the rejection of Huang, Horseblock, Hogan and Hopewell. The response asserts the prior art of record does not teach or suggest a probe of SEQ ID NO 24. This argument has been thoroughly reviewed but is not considered persuasive as Hopewell in figure 3 teaches a sequence comprising SEQ ID NO 24 and Hogan teaches methods of designing probes. Thus the combination of Huang, Horseblock, Hogan and Hopewell do render the instant claims obvious.

4. Claims 1-5, 7-10, 13, 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Horseblock et

al (WO01/70955, published September 27, 2001) and Gelfand (US Patent 5,487,972 issued Jan 30, 1996) .

This rejection is drawn to the interpretations that claim 1 requires primers consisting of SEQ ID NO 76 and SEQ ID NO 77.

Claim 5 is drawn to, "combination of oligonucleotide probes comprise the sequence identified with SEQ ID NO 24." Neither the specification nor the prior art set for a limiting definition of "the sequence identified with." Thus the broadest reasonable interpretation of, "combination of oligonucleotide probes comprise the sequence identified with SEQ ID NO 24" is any sequence that can be identified in the SEQ ID NO.

With regards to claim 1, Huang teaches a method of identifying species of bacteria in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer that amplify parE and gyrB (see column 6 lines 28-65). Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35). The nested probes are thus the equivalents of the probes claimed. Haung further teaches, "In theory, a single pair of primers, one from each flanking consensus sequence, can be used to amplify the signature sequence. However, a highly preferred embodiment includes a multiplicity of primers having sequences corresponding to potential alternate DNA sequences. As is well-known, the genetic code is degenerate, meaning that an individual amino acid may be coded for by

as many as 6 different DNA codons (each codon consisting of three adjacent nucleotides). Thus, even though the amino acid sequence of a region of type II topoisomerase from different organisms may be identical, the DNA in those organisms which codes for the region may differ. The PCR technique requires a good match between the DNA primer sequences especially at the 3' end and the DNA to which it binds (Saiki et al.). Thus, to avoid failing to amplify species having such alternate DNA sequences, the set of primers should include variant primers having at least some of the alternate sequences. Moreover, it is desirable that the amino acids in the consensus sequence be coded for by 3 or fewer different codons, especially in the portion immediately adjacent to the signature segment. Obviously, the presence of one or more amino acids having six possible codons drastically increases the number of possible DNA sequences. By choosing the consensus sequences to have amino acids with at most three possible codons (or in an even more preferred embodiment, two possible codons), the number of different oligonucleotide sequences required in the universal primers is kept manageable" (see column 7, line 60 to column 8, line 9). Huang teaches, "It will be recognized that universal primers such as the compositions described herein can be constructed for any ubiquitous protein having substantially conserved segments adjacent to variable segments. Depending upon the desired application, gene products other than type II topoisomerase might be preferable. Examples of proteins of potential use according to this invention include RNA polymerase and other DNA binding proteins. Where it is desired only to distinguish among very closely related species, a protein common only to such species may be

used" (see column 14, lines 46-50). Huang concludes, "it will be apparent how a specific primer pair for any species can be designed by the methods disclosed herein and using a database" (see column 16, lines 50-55).

With regards to claim 2, Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences due to their sequence similarities (see column 14, lines 16-19). Haung further teaches identification of legionella pneumophila (SEQ ID NO 70), which is a bacteria that infects the respiratory tract.

With regards to claim 3, Huang teaches detection of pseudomonase aeruginosa (see figure 9 a).

With regards to claim 4, Haung et al teaches the use of primers of 15 to 36 nucleotides in length (see column 7, lines 22-25).

With regards to claims 23 and 24 Huang et al teaches primers of 24 bases (see SEQ ID NO 206 and SEQ ID NO 207).

Huang does not teach primers consisting SEQ ID NO 76 and 77.

However, Horseblock et al teaches SEQ ID NO 9244, which contains nucleotides 82 to 101 that comprise SEQ ID NO 76 of instant claims. Horseblock further teaches SEQ ID NO 1844, which contains nucleotides 14 to 33 which comprise SEQ ID NO 77. Horseblock teaches, "The identified or isolated nucleic acids obtained using the PCR primers may contain part or all of the homologous nucleic acids. Because homologous nucleic acids are related but not identical in 25 sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on sequence regions that are either known to be conserved or

suspected to be conserved such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers 30 are at least 10 nucleotides, and preferably at least 20 nucleotides in length. More preferably, the PCR primers are at least 20-30 nucleotides in length. In some embodiments, the PCR primers can be more than 30 nucleotides in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same." (see page 232, lines 23-33). Horseblock teaches multiple nucleic acid sequences that comprise a multiple nucleotides that are broadly interpreted identified by SEQ ID No 24.

With regards to claims 7-9, Horseblock teaches, "In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by researchers to help identify optimal drug targets, profile new compounds, and determine disease pathway" (see page 78, lines 1-5).

With regards to claim 10, Horseblock teaches use of a single stranded labeled probe (see page 231, lines 5-20).

With regards to claim 10, Horseblock teaches the use of nucleic acid probes to identify microorganism species from clinical specimens (see page 195, line 20).

Horseblock further teaches, "Single stranded labeled cDNAs are prepared for hybridization to the array" (see page 149, line 17).

Gelfand et al. teaches a process of detecting a target nucleic acid using primers and probes in a PCR amplification assay (abstract). Gelfand et al. teaches a method comprising providing a set of oligonucleotide primers and amplifying the target nucleic acid sequence in a PCR reaction annealing both the primers and a labeled probe, and detecting the release of labeled fragments to determine the presence or absence of target sequences in the sample (column 2, lines 46-67 and column 3 lines 1-10). Gelfand teaches his method allows the amplification and detection of amplified products with minimal post-amplification handling (see column 2, lines 10-15).

Gelfand et al. provides guidance in the choosing of primers.

"The primer must be sufficiently long to prime the synthesis of extension products in the presences of the agent for polymerization. The exact length and composition of the primer will depend on many factors, including temperature of the annealing reaction, source and composition of the primer, proximity of the probe annealing site to the primer annealing site, and ration of primer: probe concentration. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains about 15-30 nucleotides, although a primer may contain more or fewer nucleotides. The primers must be sufficiently complementary to anneal to their respective strands selectively and form stable duplexes" (Column 8 lines 21-34).

Designing primers, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Gelfand. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design primers. As discussed above, the ordinary artisan would be motivated to have designed and tested new primers to obtain

additional oligonucleotides that function to detect amplify sequences and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional primers. Thus, for the reasons provided above, the ordinary artisan would have designed additional primers using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Huang with functionally equivalent primers designed by the methods of Gelfand from the nucleotide sequences Horseblock which comprise sequences identified by SEQ ID NO 76 and 77. The teachings of Gelfand and Haung would result in primers that are functional equivalents to the primers of SEQ ID NO 76 and 77. The skilled artisan would be motivated to combine the teachings of Huang, Horseblock, and Gelfand because Huang suggests the use of his method with any protein and any sequence in a database for identification of bacteria. The artisan would be motivated to make new primers for the amplification of the sequences to find primers with improved hybridization and amplification. The skilled artisan would also be motivated to combine the teachings of Huang, Horseblock, and Gelfand because Horseblock suggests the use of his method to identify microorganism species.

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use arrays or microarrays in the combined method

of Huang and Horseblock because Horseblock teaches it allows the detection of multiple gene expression products and thus markers.

The artisan would have a reasonable expectation of success in combining the teachings of Huang, Horseblock, and Gelfand as they teach methods of identifying microorganism by hybridization using methods and techniques known in the art, absent secondary considerations.

Response to arguments

This is a new ground of rejection. The arguments to the combination of Huang and Horseblock have been addressed above.

5. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Horseblock et al (WO01/70955, published September 27, 2001) and Gelfand (US Patent 5,487,972 issued Jan 30, 1996) as applied to claims 1-5, 7-10, 13, 23-24 above, and further in view of Hogan et al (US Patent 5541308) and Hopewell et al (Journal of Bacteriology (1990), volume 172, pages 3481-3484).

This rejection is drawn to the interpretation claim 5 requires a probe comprising the entire elected sequence of SEQ ID NO 24 or a sequence that is fully complementary to SEQ ID NO 24.

The teachings of Huang, Horseblock, and Gelfand are set forth in paragraph 4 above.

Huang, Horseblock, and Gelfand do not teach the probe of the comprising all or a portion of SEQ ID NO 24.

However, Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches alignment of these variable regions (see column 6 line 67—column 7, line 8). Hogan further teaches probes should be positioned to minimize stability of probe:nontarget hybrids, by avoiding GC rich regions and areas of frequent mutation (see column 7 lines 10-15). Hogan teaches the use of synthetic oligonucleotide probes of 15-50 base pairs (see column 10, lines 40-45). Hogan further teaches maximizing stability of probe target hybrid, by avoiding long AT sequences and terminating hybrids with G:C base pairing and the appropriate T_m(see column 7 lines 16-19). Hogan further teaches targeting sequences known to have secondary structure issues and probes that are self-complementary should be avoided (see column 7, lines 20-29).

Hopewell teaches sequence of Staphylococcus aureus gyrB, which comprises SEQ ID NO 24, (see figure 3B). Hopewell teaches that quinolone resistant Staphylococcus aureus are a major medical problem and this resistance is due to mutations in the DNA gyrase enzyme (see page 3481, 1st column, 1st paragraph).

Designing probes, which are equivalents to those taught in the art, is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes As discussed above, the ordinary artisan would

be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific hypervariable regions of bacteria and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the sequences provided by Horseblock using the method described by Hogan and Huang. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequence taught by Hopewell and the probe design method of Hogan to make probes to detect bacterial species based on the gyrB in the method of Huang, Horseblock, and Gelfand. The ordinary artisan would thus design a probe comprising SEQ ID NO 24 or complementary to SEQ ID NO 24. The ordinary artisan would be motivated to use the sequence taught by Hopewell to design probes by Hogan's method of probe design to identify mutations that result in quinolone resistance because Hopewell teaches this is a serious medical problem and proper identification would allow efficient treatment. The artisan would have a reasonable expectation of success as the methods are drawn to well known methods of making and analyzing nucleic acids known in the art.

Response to arguments

This is a new ground of rejection.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEVEN C. POHNERT whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/
Examiner, Art Unit 1634

Steven Pohnert